ABSTRACT

The invention describes an inexpensive *in vitro* protein folding process for preventing large scale protein misfolding and aggregation, for concentrating aggregation prone chaperonin-protein folding intermediates in a stable non-aggregating form, and for rapidly screening these stable concentrates for the best folding solution conditions. The process comprises: (1) the formation of a chaperone-substrate complex and (2) the release of the substrate using a broad array of folding solutions containing different osmolyte ions, detergents, gradients of ionic strength and pH or other commonly used folding additives. Specifically, when the chaperonin/osmolyte protein process was applied to identify and optimize GSΔ468 bacterial glutamine synthetase mutant refolding conditions that otherwise cannot be folded *in vitro* by commonly used techniques, 67% of the enzymatic activity was recovered.